HPV

Prevalence of serum antibodies to human papilloma virus in patients with genital ulcer disease in an urban population of Tanzania

J Mbwana, R Viscidi, E Lyamuya, F Mhalu, G Chalamilla, J-Å Liljeqvist, T Lagergård

Sex Transm Infect 2007;**83**:64–65. doi: 10.1136/sti.2006.021279

Background: The epidemiology of human papillomavirus (HPV) in Tanzania is largely unknown both in risk groups and in the general population.
Objective: To determine the cumulative seroprevalence of selected HPV types in order to evaluate exposure to HPV in urban Tanzania.
Method: In a cross-sectional study, sera of 200 patients of both sexes with genital ulcer disease (GUD) and sera of 60 male blood donors and 60 pregnant women were tested for antibodies to the oncogenic HPV types 16, 18, 31, 33, 35, 51 and 52 using an ELISA based on virus-like particles (VLP).
Results: The overall seroprevalence of HPV types for all patients with GUD was 83% and 77% for women and men, respectively. For pregnant women and male blood donors, the corresponding percentages were 55% and 15%, respectively. The most common HPV types were 16, 18 and 52. Infection with multiple types was more than 10 and 5 times more frequent than infection with a single type 16 in patients with GUD and in pregnant women, respectively. The seroprevalence to HPV types 16, 18, 51 and 52 was considerably higher in HIV-positive patients with GUD than in HIV-negative patients.
Conclusions: Infections with the oncogenic HPV types 16, 18 and 52 are common among patients with GUD and pregnant women in urban Tanzania, emphasising the need for control, treatment and implementation of appropriate HPV vaccine programmes.

Genital infection with human papilloma virus (HPV) is very common worldwide. Some of the HPV types, such as 16 and 18, are classified as high risk on the basis of association of infection with development of cervical cancer.[1 2] The seroprevalence of HPV 16 has varied from 10% to 52% in different studied populations;[1 4–6 8–10] however, less is known about the epidemiology and distribution of oncogenic HPV in developing countries, including Tanzania.

We used an HPV VLP-based ELISA to investigate the cumulative seroprevalence of oncogenic HPV types 16, 18, 31, 33, 35, 51 and 52 in female and male patients with genital ulcers (GUD), pregnant women and male blood donors from an urban population in Tanzania.

METHODS

Study populations

Sera were collected from 200 patients with genital ulcers (115 women and 85 men), who presented at sexually transmitted infection clinics in two cities in Tanzania. All the sera were tested for HIV antibodies as described.[3] The overall HIV seroprevalence in patients with GUD was 65% and 58% for women and men, respectively. For comparison, 60 serum samples from pregnant women and 60 from male blood donors, all HIV seronegative, representing a healthy population from the same area, were investigated.

HPV VLP ELISA serology

Previously described ELISA with HPV VLPs[4–8] was used to determine antibodies to HPV 16, 18, 31 33, 35, 51 and 52. A positive and negative reference serum pool was selected from patients with moderate levels of antibodies to all tested serotypes and from children, respectively. A positive antibody level was defined and based on an optical density absorbance value that was greater than the mean of the negative control group plus three SDs for each HPV protein tested (cut-off $\geqslant 0.3$).[4]

Statistical analysis

Power calculations were performed for the available sample size according to the studied population (patients with GUD) to ensure sufficient statistical power to detect a 2–3-fold increase in the proportion of seropositivity compared with pregnant women and male blood donors.

The differences in proportion between the studied groups were calculated by Fisher's exact test (two-tailed).

RESULTS

The overall seroprevalence to all seven HPV types among patients with GUD in Tanzania was 80%: 83% in women and 77% in men. Corresponding values for pregnant women and male blood donors were 55% and 15%, respectively. In patients with GUD and in pregnant women, the most prevalent antibodies detected were against HPV types 16, 18 and 52 (table 1), and this seroprevalence was considerably higher in female than in male patients with GUD.

The seropositivity to multiple types was higher than that to a single type in patients with GUD and pregnant women—for example, to type 16, being 58% and 5.5%, and 40 and 8.3, respectively.

The overall seroprevalences of HPV in HIV-positive and HIV-negative patients with GUD were similar, being 84% and 76%, respectively. However, the HIV-positive female patients with GUD showed a significantly higher prevalence of antibodies to types 51 and 52 than the HIV-negative female patients. Significantly higher seropositivity was observed for types 16, 35, 51 and 52 for HIV-positive males with GUD compared with HIV-negative males.

DISCUSSION

The study showed that in Tanzania the overall seroprevalence of oncogenic HPV, especially type 16, is very high in patients

Abbreviations: GUD, genital ulcer disease; HPV, human papillomavirus; VLP, virus-like particles

Table 1 Prevalence of seropositivity to seven human papillomavirus types among patients with genital ulcer disease with respect to gender, pregnantwomen and male blood donors

	Total prevalence of GUD (n = 200)	Females with GUD (n = 115)	Pregnant women (n = 60)	Females with GUD v pregnant women	Males with GUD (n = 85)	Blood donors (n = 60)	Males with GUD v blood donors
HPV types	n (%)	n (%)	n (%)	p Value	n (%)	n (%)	p Value
16	115 (58)	80 (69)	24 (40)	0.001	35 (41)	6 (10)	0.001
18	57 (29)	44 (38)	7 (12)	0.001	13 (15)	3 (5)	0.05
31	0 (0)	0 (0)	0 (0)	ND	0 (0)	0 (0)	ND
33	6 (3)	5 (4)	0 (0)	NS	1 (1)	0 (0)	ND
35	20 (10)	9 (8)	1 (2)	NS	11 (13)	1 (2)	0.03
51	36 (18)	24 (21)	5 (8)	0.03	12 (14)	2 (3)	0.03
52	122 (61)	83 (72)	23 (38)	0.001	39 (46)	1(2)	0
All	160 (80)	84 (83)¶	33 (55)††	NS	66 (77)**	9 (15)‡‡	0.001

GUD, genital ulcer disease;ND, not determined.
The p values were calculated using the two-tailed Fisher's exact test.
¶ vs. ** =NS and †† vs. ‡‡ = <0.001.

with GUD, as well as in pregnant women, indicating high overall exposure to HPV. In another study from Tanzania, where cervical HPV DNA detection was used, an HPV prevalence of 34% was observed among pregnant women from Mwanza.[9] A comparable, high seroprevalence rate of HPV 16, 68% and 70%, was noted in South Africa in HIV-positive and HIV-negative female sex workers, respectively.[7] In contrast, in patients in developed countries —for example, the United States—the seroprevalence of HPV 16 was more than two times lower for patients attending sexually transmitted infection clinics and for pregnant women.[4–6]

The high prevalence of multiple HPV seroreactivity in women observed here and in other studies has been associated with cumulative exposure to HPV rather than crossreactivity,[8] although some crossreactivity between related types cannot be ruled out.

Previous studies have shown some geographical differences in HPV type distribution,[1 2] and knowledge of such distributions in a particular population has important consequences for vaccine development against HPV. In this study, HPV 52 was slightly more prevalent than HPV 16 among patients with GUD of both sexes. However, HPV 16 was the most prevalent type in other world regions reported.[1 2] HPV 52 was found slightly more frequently than types 16 and 35 in Kenya among attendees at family planning clinics.[10] The similar HPV seroprevalence noted in Tanzania and Kenya may be due to the free movement of people between these two neighbouring countries.

ACKNOWLEDGEMENTS

This work was supported by the Swedish Agency for Research Cooperation with Developing Countries (SIDA/Sarec). We thank the clinicians at Igawilo, Kiwanjampaka, Ruanda Health Centres and Mbeya Referral Hospital, laboratory staff at Mbeya Referral Hospital and the Department of Microbiology and Immunology, Muhimbili National Hospital, for technical support and Valter Sundh for the statistical evaluation. This study was conducted with the approval of the institutional ethics research committees at the Muhimbili University College of Health Sciences, Dar es Salaam, Tanzania.

Authors' affiliations

J Mbwana, J-Å Liljeqvist, T Lagergård, Institute of Biomedicine, The Sahlgrenska Academy at Göteborg University, Göteborg, Sweden
R Viscidi, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
E Lyamuya, F Mhalu, Department of Medical Microbiology and Immunology, Muhimbili University College of Health Sciences, Dar es Salaam, Tanzania
G Chalamilla, The Infectious Diseases Clinic, Dar es Salaam, Tanzania

Competing interests: None declared.

Correspondence to: Professor T Lagergård, Institute of Biomedicine, Department of Microbiology and Immunology, The Sahlgrenska Academy at Göteborg University, Box 435, S-405 30 Göteborg, Sweden; teresa.lagergard@microbio.gu.se

Accepted 1 June 2006
Published Online First 28 June 2006

REFERENCES

1 **Clifford GM**, Gallus S, Herrero R, *et al*. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. *Lancet* 2005;**366**:991–8.
2 **Munoz N**, Bosch FX, de Sanjose S, *et al*. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med* 2003;**348**:518–27.
3 **Ahmed HJ**, Mbwana J, Gunnarsson E, *et al*. Etiology of genital ulcer disease and association with human immunodeficiency virus infection in two Tanzanian cities. *Sex Transm Dis* 2003;**30**:114–19.
4 **Viscidi RP**, Ahdieh-Grant L, Clayman B, *et al*. Serum immunoglobulin G response to human papillomavirus type 16 virus-like particles in human immunodeficiency virus (HIV)-positive and risk-matched HIV-negative women. *J Infect Dis* 2003;**187**:194–205.
5 **Thompson DL**, Douglas JM Jr, Foster M, *et al*. Seroepidemiology of infection with human papillomavirus 16, in men and women attending sexually transmitted disease clinics in the United States. *J Infect Dis* 2004;**190**:1563–74.
6 **Hagensee ME**, Slavinsky J III, Gaffga CM, *et al*. Seroprevalence of human papillomavirus type 16 in pregnant women. *Obstet Gynecol* 1999;**94**:653–8.
7 **Marais DJ**, Vardas E, Ramjee G, *et al*. The impact of human immunodeficiency virus type 1 status on human papilloma virus (HPV) prevalence and HPV antibodies in serum and cervical secretions. *J Infect Dis*, 2000;1239–42..
8 **Combita AL**, Bravo MM, Touze A, *et al*. Serologic response to human oncogenic papillomavirus types 16, 18, 31, 33, 39, 58 and 59 virus-like particles in colombian women with invasive cervical cancer. *Int J Cancer* 2002;**97**:796–803.
9 **Mayaud P**, Weiss HA, Lacey CJ, *et al*. Genital human papillomavirus genotypes in northwestern Tanzania. *J Clin Microbiol* 2003;**41**:4451–3.
10 **De Vuyst H**, Steyaert S, Van Renterghem L, *et al*. Distribution of human papillomavirus in a family planning population in Nairobi, Kenya. *Sex Transm Dis* 2003;**30**:137–42.